## REMARKS

Applicants have amended Claim 1. Enabling support for the amendment can be found in the application as filed, and therefore no new matter is contained in the amendment. Reconsideration of the present application and allowance of resulting Claims 1 through 4 is respectfully requested in view of the amendment and the following remarks.

### I. Claim Rejections Under 35 U.S.C. § 112, first paragraph

The Office Action rejected Claims 1-4 under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement by the addition of new matter. The Office Action stated that the sections of the specification cited by Applicants in their response to the previous Office Action did not contain support for the new limitation that the DNA vector be "non-viral." Applicants respectfully submit that the previous amendments to Claims 1, 2, and 4 do not include new matter.

Applicants respectfully submit that the specification as filed provides support for the addition of the term "non-viral" to the claims. In particular, Applicants submit that the specification contains such support on page 7, lines 3-4. For example, the specification notes that "[t]he vector pIRES/EGFP ... of the present invention is that which is described in the Examples section under Methods (DNA Constructs)." Applicants note that the vector described under the Methods (DNA Constructs) section describes a *non-viral* DNA vector construct that was created by subcloning the EGFP coding sequence from the pEGFP plasmid vector into the pIRES plasmid vector. (See page 12, line 25 to page 13, line 13.) This non-viral DNA vector construct places the neomycin resistance gene and the EGFP gene sequences under the control of a single promoter, the human cytomegalovirus (CMV) promoter.

In addition, Applicants submit further support may be found in the specification on page 7, lines 18-21. This sentence specifies that the cloning of the fragment of pIRES/EGFP vector which contains the pIRES and the EGFP gene into a viral vector is a *modification* of the original pIRES/EGFP vector. As sufficient support for the term "non-viral" is present in the specification

as filed, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

## II. Claim Rejections Under 35 U.S.C. § 102

The Office Action rejected Claims 1, 2, and 4 under 35 U.S.C. § 102(b) as being anticipated by Clontech Catalog #6064-1 (pIRES-EGFP Vector Information, © 1997). The Office action stated that the reference teaches a non-viral DNA vector comprising an IRES, a selection marker ($Amp^r$), and a green fluorescent protein and that the reference teaches that the vector could be used to obtain stably transfected cell lines. Applicants respectfully submit that the rejections of Claims 1, 2, and 4, as being anticipated by the Clontech Catalog #6064-1 reference, are rendered moot by the present amendment to the claims.

Claim 1 has been amended to require that the selection marker sequence and the green fluorescent protein gene sequence must be transcribed as a single mRNA transcript. Support for this amendment may be found in the specification, for example, on page 13, lines 5-12. The Clontech Catalog #6064-1 reference teaches a non-viral DNA vector where the selection marker ($Amp^r$) is transcribed under the control of a different promoter than the green fluorescent protein gene. Therefore, Applicants respectfully submit that amended Claim 1 is not anticipated by the Clontech Catalog #6064-1 reference. Because Claims 2 and 4 depend from amended Claim 1, Applicants respectfully submit that Claims 2 and 4 also are not anticipated by the Clontech Catalog #6064-1 reference. Accordingly, Applicants respectfully request that the rejections of Claims 1, 2, and 4 under 35 U.S.C. § 102(b) as being anticipated by Clontech Catalog #6064-1 be withdrawn.

The Office Action rejected Claims 1, 2, and 4 under 35 U.S.C. § 102(b) as being anticipated by CLONTECHniques (April 1998). The Office action stated that the CLONTECHniques reference teaches a non-viral DNA vector comprising an IRES, a selection marker ($Amp^r$), and a green fluorescent protein and that the reference teaches that the vector could be used to select stably transfected mammalian cells. Applicants respectfully submit that the rejections of Claims 1, 2, and 4, as being anticipated by the CLONTECHniques reference, are rendered moot by the present amendment to the claims.

As discussed above, Claim 1 has been amended to require that the selection marker sequence and the green fluorescent protein gene sequence must be transcribed as a single mRNA transcript, and Claims 2 and 4 depend from amended Claim 1. The CLONTECHniques reference teaches a non-viral DNA vector where the selection marker ($Amp^r$) is transcribed under the control of a different promoter than the green fluorescent protein gene. The CLONTECHniques reference further teaches IRES expression vectors that contain *either* a drug resistance marker *or* a fluorescent protein, located after the IRES site, but the reference does not teach a vector in which both a selection marker sequence and the green fluorescent protein sequence are transcribed as a single RNA transcript. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) as being anticipated by the CLONTECHniques reference be withdrawn.

The Office Action rejected Claims 1, 2, and 4 under 35 U.S.C. § 102(b) as being anticipated by Mosser et al. (Biotechniques (1997) 22(1):150-161). The Office action stated that the reference teaches a non-viral DNA vector construct comprising an IRES, a selection marker ($Amp^r$), and a green fluorescent protein and that the reference teaches that the vector could be used to obtain clones that stably express the desired gene product. Applicants respectfully submit that the rejections of Claims 1, 2, and 4, as being anticipated by Mosser et al. reference, are rendered moot by the present amendment to the claims.

As discussed above, Claim 1 has been amended to require that the selection marker sequence and the green fluorescent protein gene sequence must be transcribed as a single mRNA transcript, and Claims 2 and 4 depend from amended Claim 1. The Mosser et al. reference teaches a non-viral DNA vector where the selection marker ($Amp^r$) is transcribed as a monocistronic transcript under the control of a different promoter than the green fluorescent protein gene. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) as being anticipated by the Mosser et al. reference be withdrawn.

## III. Claim Rejections Under 35 U.S.C. § 103

The Office Action rejected Claims 1, 2, 3, and 4 under 35 U.S.C. § 103(a) as being unpatentable over the Clontech reference, the CLONTECHniques reference, or the Mosser et al. reference, in view of the Cheng et al. reference (Gene Therapy (1997) 4:1013-1022). The Office

action stated that the Clontech reference, the CLONTECHniques reference, and the Mosser et al. reference all teach a non-viral DNA vector construct comprising an IRES, a selection marker, and a green fluorescent protein and that the vector could be used to obtain stably transfected cells or cell lines. The Office Action also stated that Cheng et al. teach a DNA vector construct comprising an IRES, a selection marker, and a green fluorescent protein; stably transfected cells with the vector; and stable transfection of stem cells. Applicants respectfully submit that Claims 1-4, as amended, are not obvious over the Clontech reference, the CLONTECHniques reference, or the Mosser et al. reference, in view of the Cheng et al. reference.

"Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed. Cir. 1984). Applicants respectfully submit that the prior art does not provide the necessary teaching, suggestion, or incentive to combine the teachings of the cited references to arrive at the present invention. The present invention relates to a non-viral vector comprising a selection marker and a green fluorescent protein gene that are transcribed as a single mRNA transcript. The present application discloses that such a non-viral vector is useful to efficiently create stably transfected cells which comprise the vector and that the dicistronic expression of the selection marker and a green fluorescent protein genes of the present invention allows for the simplified selection and maintenance of positive transfectants. The present invention also discloses that the use of this vector allows one to effectively monitor cell motility, and in particular, stem cell and tumor cell migration. The genes on the non-viral DNA vector construct of the present invention are stably expressed in the transfected cells.

Cheng et al. describe the transduction of hematopoietic stem cells with a retroviral vector comprising the EGFP gene in order to develop a reporter system for optimum retrovirus-mediated gene transfer into human primitive hematopoietic progenitors. The retroviral vectors were chosen as a "primary choice as a vehicle for gene delivery since they are capable of integrating into cellular chromosomes, resulting in stable transmission to every progeny cell derived from transduced [hematopoietic stem and progenitor cells]." (*See* Cheng et al., page 1013, column 1.) Therefore, the Cheng et al. reference can be said to teach away from the presently claimed invention using non-viral DNA vector construct. There are many

disadvantages of using a retroviral vector system as has been discussed previously. For example, transduction procedure is lengthy and cumbersome; the integration of the retroviral vector DNA into the host cell DNA is random; non-native DNA sequences may be excised from the chromosomal DNA at a high rate; and retroviral genes may elicit an immune response in a host organism. The Clontech reference, the CLONTECHniques reference, and the Mosser et al. reference suggest the use of non-viral vectors comprising an IRES and a green fluorescent protein to obtain stably transfected cells or cell lines. However, none of these references suggest that the use of a selection marker and a green fluorescent protein as a dicistronic transcript would allow a means for the efficient selection and monitoring of transfectants.

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP §2143.01, *citing In re Mills*, 916 F.2d 680 (Fed. Cir. 1990). Despite the longfelt need for improved systems for transfecting cells for monitoring cellular motility, there has been no suggestion of achieving the same with the advantages of the presently claimed compositions. Applicants respectfully submit that the Office Action applies hindsight analysis to consider the combination of the cited references to render the claimed invention obvious, and that one of ordinary skill in the art at the time of this invention would not have been prompted to combine the teachings of these references to arrive at the present invention. Accordingly, Applicants respectfully request that the rejections of Claims 1-4 under § 103 be withdrawn.

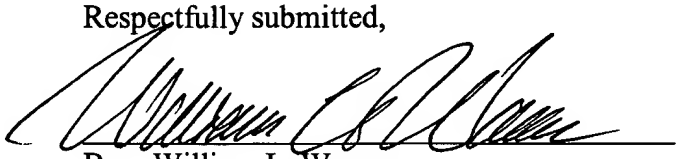
## IV. Concluding Remarks

For at least the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejections and allowance of Claims 1-4. The foregoing is submitted as a full and complete Response to the Office Action mailed February 19, 2004.

A Request for Continued Examination pursuant to 37 C.F.R. § 1.114 and a check in the amount of $385 are being submitted herewith. In addition, a petition for a three month extension of time, as well as fees in the amount of $475, are being submitted concurrently herewith. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to Deposit Account No. 19-5029.

This Response places all claims in the present application in condition for allowance, and such action is courteously solicited. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,



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